## REMARKS

### SPECIFICATION

Applicants have amended the specification with respect to the use of trademarks and brackets. With respect to the use of brackets on page 33 and 34, Applicants submit that the brackets are necessary for clearly describing the name of the chemical compounds, therefore, no amendment was made to remove the brackets on these two pages.

### CLAIMS

Claims 1-29 are currently pending in the application. No claims are amended, no new matter is added.

Claim Rejections under 35 U.S.C. § 102(b) over Kwok et al.

Claims 12-13 and 26 are rejected under 35 U.S.C. § 102 as alleged being anticipated by Kwok et al. (U.S. Patent No. 5,945,283). The Office Action states that Kwok et al, teach a composition and kit for identifying a target nucleotide sequence in a sample, the composition and kit comprising an oligonucleotide sequence comprising a first sequence which hybridizes to the target polynucleotide immediately 3' of the target sequence, and is covalently attached to a tag molecule; *and an anti-tag molecule which binds to said tag molecule,* said anti-tag molecule labeled with a first member of a pair of interactive labels. The Office Action also states that Kwok et al. also teach packaging material thereof. In addition, the Office Action states that Kwok et al. discloses that the tag is located on the 5' terminal of said oligonucleotide primer. The Office Action, therefore, concludes that claims 12-13 and 26 are anticipated by Kwok et al.

Applicants respectfully disagree.

Claim 12 (its dependent claim 13) and claim 26 of the present invention are drawn to a composition (claim 12) or a kit (claim 26) for identifying a nucleotide at a predetermined position of a target polynucleotide in a sample, said composition comprising: (a) an oligonucleotide primer comprising a first sequence which hybridizes to the target polynucleotide immediately 3' of said nucleotide, and is covalently attached to a tag molecule; and (b) ***an anti-***

***tag molecule which binds to said tag molecule***, said anti-tag molecule labeled with a first member of a pair of interactive labels.

The present specification provides the following definitions for "tag molecule" and "anti-tag molecule:"

> "A 'tag molecule' refers to a molecule covalently coupled to an oligonucleotide primer. ***An "anti-tag molecule" refers to a molecule which interacts with the tag molecule through specific binding.*** An anti-tag molecule useful in the invention may be further labeled with a member of a pair of interactive labels. The tag and anti-tag molecule pair allows the interaction of a labeled anti-tag molecule with an oligonucleotide primer which may comprise an incorporated labeled polynucleotide chain terminator. ***A tag molecule and its corresponding anti-tag molecule, according to the invention, can be members of a specific binding pair***. It is not critical for either a tag molecule or an anti-tag molecule to be a specific member of a specific binding pair, so long as it permits the binding between the members of the specific binding pair." (page 15, lines 10-19)

The present specification further teaches:

> "As used herein, a "specific binding pair" refers to two different molecules, where ***one molecule has an area on the surface or in a cavity which specifically binds to and is thereby defined as complementary with a particular spatial and polar organization of the other molecule***. The two molecules of a specific binding pair may also comprise complementary sequences and form the specific binding through base-pairing. A "specific binding pair", according to the invention, include, but are not limited to members of an immunological pair such as antigen-antibody, or an operator-repressor, nuclease-nucleotide, biotin-streptavidin, ligand-receptor pair, polynucleotide duplexes, IgG-protein A, DNA-DNA, DNA-RNA." (page 15, lines 20-27)

It is clear from the teaching of the present specification that the anti-tag molecule and the tag molecule, as recited in claims 12-13 and 26, ***specifically bind to each other***, for example, as members of a specific binding pair.

There is no teaching in Kwok et al. regarding an anti-tag molecule that binds to a tag molecule, which binds to the target polynucleotide. In contrast, Kwok et al. teaches a polynucleotide covalently linked to one fluorophore (i.e., the labeled polybucleotide), which is capable of binding to the target site of the target polynucleotide, and ***a dideoxynucleotide*** (covalently linked to a second fluorophore), which is ***capable of binding to the target nucleotide in the target polynucleotide*** at a different position. Therefore, ***both the labeled polynucleotide and dideoxynucleotide bind to the target polynucleotide template.*** There is no teaching that the dideoxynucleotide binds to the labeled polynucleotide. Therefore, there is ***no specific binding*** relationship between the dideoxynucleotide and the labeled polynucleotide, as required for the tag and anti-tag molecules of claims 12-13 and 26 of the present invention.

Therefore, Kwok et al. does not teach the requirement of "an anti-tag molecule which binds to said tag molecule," as recited in claims 12-13 and 26. Kwok et al. does not anticipate the invention of claims 12-13 and 26. Applicants respectfully request the 102(b) rejections on claims 12-13 and 26 be withdrawn.

Claim Rejections under 35 U.S.C. § 102(a) and 102(e) over Nadeau et al.

Claims 1, 17, and 19 are rejected under 35 U.S.C. § 102(a) and 102(e) for lack of novelty over Nadeau et al. (U.S. Patent No. 6,316,200B1. The Office Action states that Nadeau et al. teach a composition for identifying a target sequence in a sample, the composition comprising (a) an oligonucleotide primer comprising a sequence which hybridizes to a complementary sequence 3' of the target nucleic acid and a second sequence which does not hybridize to said target polynucleotide in the presence of a third sequence; and (b) *an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide,* said oligonucleotide probe labeled with a first member of a pair of interactive labels. The Office Action also states that Nadeau et al. teaches the second sequence is on the 5' end of the first sequence. The Office Action further states that Naseau et al. teaches that one

member of the pair of interactive labels is a quencher molecule. The Office Action, therefore, concludes that claims 1, 17, and 19 are anticipated by Nadeau et al.

Applicants respectfully disagree.

Claims 1, 17 and 19 of the present invention are drawn to a composition for identifying a nucleotide at a predetermined position of a target polynucleotide in a sample, said composition comprising: (a) an oligonucleotide primer comprising a first sequence which hybridizes to said target polynucleotide immediately 3' of said nucleotide, and a second sequence which does not hybridize to said target polynucleotide in the presence of a third sequence; and (b) ***an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide primer***, said oligonucleotide probe labeled with a first member of a pair of interactive labels. The invention as recited in claims 1, 17, and 19 require an oligonucleotide probe to hybridize to the second sequence of the oligonucleotide primer, where the second sequence itself does not hybridize to the target polynucleotide.

The present specification defines "oligonucleotide primer" and "oligonucleotide probe" as follows:

"As used herein, an 'oligonucleotide primer' is an oligonucleotide comprising a sequence complementary to a target polynucleotide. An oligonucleotide, according to the invention, hybridizes to a target polynucleotide through base pairing so to initiate an elongation (extension) reaction to incorporate a nucleotide into the oligonucleotide primer. An "oligonucleotide primer" according to the present invention, may comprise a first sequence that hybridizes to a target polynucleotide immediately 3' of a nucleotide at a predetermined location. ***An 'oligonucleotide primer' may comprise a first sequence which hybridizes to a target polynucleotide and a second sequence which does not hybridize to the target polynucleotide in the presence of a third sequence.*** The first sequence or the second sequence of an oligonucleotide may be between 10 to 100 nucleotides in length, preferably between 15-50 nucleotides in length. A common second sequence may be used for a number of oligonucleotide primers comprising the same first sequence. An oligonucleotide primer useful in the present invention may be covalently coupled to a tag molecule.

***An 'oligonucleotide probe' is an oligonucleotide comprising a third sequence which is complementary to the oligonucleotide primer***. One or more oligonucleotide probes can be made, each comprising a different sequence complementary to the oligonucleotide primer. An "oligonucleotide probe" according to the invention, may be between 10 to 100 nucleotides in length, preferably between 15-50 nucleotides in length. When an oligonucleotide probe is designed to ***complement to a common second sequence*** on a number of oligonucleotide primers, the oligonucleotide probe is also referred to as a universal probe for the number of oligonucleotide primers." (page 14, lines 8-28)

The invention, as recited in claims 1, 17 and 19, require that the oligonucleotide probe ***itself,*** not its complementary sequence, to comprise a sequence that hybridizes to the second sequence of the oligonucleotide primer. Such requirement is consistent with the teachings in the present specification as described above herein.

Nadeau et al. does not teach an oligonucleotide probe which itself hybridizes to the oligonucleotide primer. In contrast, Nadeau et al. teaches an adapter sequence on the signal primer "is selected such that its ***complementary sequence*** will hybridize to the 3' end of the reporter probe..." (column 4, line 55), and that "[t]he sequence of the reporter probe 3' to the reporter moiety is selected to hybridize to the ***complement*** of the signal primer adapter sequence." (column 5, lines 3-6) Therefore, the probe in Nadeau et al. does not directly hybridize to the primer at all, it only hybridizes to the complemenary sequence of the primer.

Nadaeu et al., therefore, does not teach ***an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide primer***, as required by claims 1, 17, and 19. Therefore, Nadaeu et al. can not anticipate the invention of claims 1, 17 and 19. Applicants respectfully request the 102(a) and 102(e) rejections on claims 1, 17, and 19 be withdrawn.

Claim Rejections under 35 U.S.C. § 102(a) and 102(e) over Huang et al.

Claims 1, 12-16, 20 and 26-29 are rejected under 35 U.S.C. § 102(a) and 102(e) as being anticipated by Huang et al. (U.S. Patent No. 6,287,778B1). The Office Action states that Huang

et al. teaches a composition and kit for the identification of nucleotides at a predetermined position in a nucleic acid sample, the composition and kit comprising an oligonucleotide primer comprising a sequence which hybridizes to the target polynucleotide immediately 3' of the target nucleic acid sequence and a second sequence which does not hybridize to said target polynucleotide in the presence of a third sequence; and an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide, *said oligonucleotide probe labeled with a first member of a pair of interactive labels*. The Office Action states that Huang et al, teaches a composition and kit for the identification of nucleotides at a predetermined position in a nucleic acid sample, the composition and kit comprising an oligonucleotide primer comprising a first sequence which hybridizes to the target polynucleotide immediately 3' of the target nucleic acid sequence, and an anti-tag molecule which binds to said tag molecule, *said anti-tag molecule labeled with a first member of a pair of interactive labels*. The Office Action states that Huang et al. also discloses the composition and kit of claims 12 and 26, wherein said tag molecule may comprise a first member of a specific binding pair and wherein *said anti-tag molecule may comprise the second member of a specific binding pair*, wherein said specific binding pair is a biotin-streptavidin pair.

Applicants respectfully disagree.

Claims 1 and 20 of the present invention are drawn to a composition and kit for identifying a nucleotide at a predetermined position of a target polynucleotide in a sample, said composition comprising: (a) an oligonucleotide primer comprising a first sequence which hybridizes to said target polynucleotide immediately 3' of said nucleotide, and a second sequence which does not hybridize to said target polynucleotide in the presence of a third sequence; and (b) an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide primer, ***said oligonucleotide probe labeled with a first member of a pair of interactive labels.***

Claim 12, its dependent claim 13, and claim 26 of the present invention are drawn to a composition (claim 12) or a kit (claim 26) for identifying a nucleotide at a predetermined position of a target polynucleotide in a sample, said composition comprising: (a) an

oligonucleotide primer comprising a first sequence which hybridizes to the target polynucleotide immediately 3' of said nucleotide, and is covalently attached to a tag molecule; and (b) an anti-tag molecule which binds to said tag molecule, said anti-tag molecule labeled with a first member of a pair of interactive labels.

Claim 14 (depending from claim 12) and claim 27 (depending from claim 26) are additionally drawn to said tag molecule is a first member of a specific binding pair which comprises said first member and a second member. Claim 15 (depending from claim 12) and claim 28 (depending from claim 26) are additionally drawn to said anti-tag molecule is said second member of said specific binding pair. Claim 16 (depending from claim 12) and claim 29 (depending from claim 26) are additionally drawn to said specific binding pair comprises a biotin-streptavidin pair.

Applicants submits that Huang et al. does not teach ***a pair of interactive labels,*** or ***an oligonucleotide probe labeled with a first member of a pair of interactive labels*** as recited in claims 1 and 20, and the dependent claims 14-16. Neither does Huang et al teach ***an anti-tag molecule labeled with a first member of a pair of interactive labels*** as recited in claim 26 and its dependent claims 27-29.

Huang et al. teaches a method for determining the genotype of one or more individuals at a polymorphic locus employs amplification of a region of DNA, labeling of allele-specific extension primers containing tags, and hybridization of the products to an array of probes (see abstract). The method comprises steps of: amplifying a region of DNA in the sample, wherein the region comprises a polymorphic locus of the selected allele of the gene, to form an amplified DNA product; ***labeling an extension primer*** in the presence of the amplified DNA product, wherein the amplified DNA product serves as a template for the step of labeling, wherein the extension primer comprises a 3' portion which is complementary to the amplified DNA product and a 5' portion which is not complementary to the amplified DNA product, wherein the extension primer terminates in a 3' nucleotide at the polymorphic locus of the selected allele, whereby at least ***one labeled nucleotide*** is coupled to the 3' terminal nucleotide of the extension primer to form a labeled extension primer; and hybridizing the labeled extension primer to a

probe on a solid support, wherein at least a portion of the probe is complementary to the 5' portion of the extension primer (see claim 1 for example).

In the above method taught by Huang et al., the incorporated nucleotide is labeled to form a labeled extension primer (also see column 8, line 50 to column 9, line 60). The labeled extension primer hybridizes to a probe on a solid support and the hybridization is detected based on the label on the extension primer (see column 16, lines 42-49). Huang et al. teaches:

> "The extension primer has two portions, a 3' portion which is complementary to a portion of the region of double stranded DNA which contains the polymorphic locus and a 5' portion which is not complementary to the region of double stranded DNA. The 5' region is the tag sequence which is complementary to the ***tag array*** which is used to sort and analyze the products of the primer extension reaction. The 3' end of the extension primer terminates at the polymorphic locus." (column 6, lines 12-20)

Huang et al, however, ***does not teach a labeled probe***. In Huang et al., the tag array (i.e., probe) is not labeled and does not provide any signal in the detection. In addition, Huang et al. does not teach ***a member of a pair of interactive labels*** as recited in the claims of the present application.

Therefore, Huang et al. does not anticipate claims 1, 12, 20, 26 and their dependent claims 13-16 and 27-29 of the present application, which require that ***the probe or the anti-tag molecule is labeled with a first member of a pair of interactive labels***. Applicants respectfully request the 102 rejections on claims 1, 12-16, 20, and 26-29 be withdrawn.

Claim Rejections under 35 U.S.C. § 103(a) over Nadeau et al. in view of Goelet et al.

Claims 2-6, 8-11, and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nadaeu et al. as applied to clams 1, 17 and 19 above in view of Goelet et al. (U.S. Patent No. 5,888,819). The Office Action mentions claim 18 in the same paragraph, but it is unclear whether claim 18 is included in the rejection. Applicants, however, have included claim 18 in the response.

The Office Action states that Nadaeu et al. teach a composition comprising for detecting a target nucleotide sequence in a sample, the composition comprising an oligonucleotide sequence which hybridizes to said target polynucleotide immediately 3' of the target sequence, a second sequence which does not hybridize to said target polynucleotide in presence of a third sequence; and *oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide sequence*, said oligonucleotide probe labeled with a first member of a pair of interactive labels. The Office Action states that Goelet et al. teaches a composition and kit comprising an oligonucleotide primer comprising a sequence which hybridizes to said target polynucleotide immediately 3' of a target nucleotide sequence and a first, second, third, and fourth polynucleotide terminator that are not identical, which is incorporated in a template-dependent manner into said oligonucleotide primer by a polynucleotide synthesis enzyme; that Goelet et al. further teaches wherein the first, second, third, and fourth polynucleotide terminators are labeled with a detectable marker, wherein the detectable marker may be a fluorophore or a moiety to which an isotopically labeled moiety such as a fluorophore can be attached; and that Goelet et al. further teaches that using all four terminators comprising different detectable markers ensures fidelity, i.e., suppression of misleading and that the sequence of the extended primer can be deduced and more than one reaction product can be analyzed per reaction if more than one terminator is specifically labeled. The Office Action then relied on the alleged teaching of Kwok et al. on composition and kit comprising an oligonucleotide sequence comprising a first sequence which hybridizes to the target polynucleotide immediately 3' of the target sequence and is covalently attached to a tag molecule; and *an anti-tag molecule which binds to said tag molecule*, said anti-tag molecule labeled with a first member of a pair of interactive labeled and that the composition comprises a first, second, third and/or fourth polynucleotide terminator labeled with a first member of a pair of interactive label which interacts with a second member of a pair of interactive labels to generate a signal by fluorescent resonance energy transfer, and that the composition comprising polynucleotide terminators labeled with a pair of interactive labels for use in methods of detecting a target polynucleotide sequence is advantageous because it allows the detection of a target nucleotide sequence to be accomplished in one reaction vessel without the requirement for

separation or purification step. The Office Action then concludes that one skilled in the art would have been motivated to "do so or the advantages taught by Kwok et al."

Applicants respectfully disagree.

First, contrary to the Examiner's assertion, Kwok et al. ***does not teach an anti-tag molecule that binds to a tag molecule***. Kwok et al. teaches a polynucleotide covalently linked to one fluorophore (i.e., the labeled polybucleotide), which is capable of binding to the target site of the target polynucleotide, and a dideoxynucleotide (covalently linked to a second fluorophore), which is also capable of binding to the target nucleotide in the target polynucleotide at a different position. The advantage recognized in Kwok et al. at the time of filing (1996), i.e., a composition which allows the detection of a target nucleotide sequence to be accomplished in one reaction vessel without the requirement for separation or purification step, is simply ***a recognized need in the art***, which both Kwok et al. and Applicants of the present application try to accomplish using different approaches.

Second, unlike the Examiner's characterization, the primary reference Nadaeu et al. ***does not teach*** an element required in claims 2-6, 8-11, 18, and 21-24 of the present application, i.e., ***an oligonucleotide probe comprising said third sequence which hybridize to said second sequence of said oligonucleotide primer***. In contrast, Nadaeu et al. teaches an adapter sequence on the signal primer "is selected such that its ***complementary sequence*** will hybridize to the 3' end of the reporter probe..." (column 4, line 55), and that "[t]he sequence of the reporter probe 3' to the reporter moiety is selected to hybridize to the ***complement*** of the signal primer adapter sequence." (column 5, lines 3-6) Therefore, the probe in Nadeau et al. does not hybridize directly to the primer at all, it hybridizes to the complementary sequence of the primer. The secondary reference, Goelet et al., does not remedy this deficient teaching of Nadaeu et al. with respect to an oligonucleotide probe comprising the third sequence which hybridize to the second sequence of the oligonucleotide primer.

Therefore, absent the teaching in the present application, even one skilled in the art recognizing the need as stated in Kwok et al., such as in the composition taught by Nadeau et al., would not have been motivated to include a specific "***oligonucleotide probe comprising said***

***third sequence which hybridize to said second sequence of said oligonucleotide primer***" as required by claims 2-6, 8-11, 18 and 21-24. The combination of Nadeau et al. and Goelet et al. would not have arrived to the present invention, which requires "an oligonucleotide probe comprising said third sequence which hybridize to said second sequence of said oligonucleotide primer."

Therefore, claims 2-6, 8-11, 18 and 21-24 are not obvious over Nadeau et al. in view of Goelet et al. Applicants respectfully request the 103(a) rejections as to the above claims be withdrawn.

Claim Rejections under 35 U.S.C. § 103(a) over Nadeau et al. in view of Soderlund et al.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nadaeu et al. as applied above in view of Soderlund et al. (U.S. Patent No. 6,013,431). The Office Action reiterates its position on Nadaeu et al. that it teaches a composition for detecting a target nucleotide sequence in a sample, the composition comprising an oligonucleotide sequence which hybridizes to said target polynucleotide immediately 3' of the target sequence, a second sequence which does not hybridize to said target polynucleotide in presence of a third sequence; and *oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide sequence*, said oligonucleotide probe labeled with a first member of a pair of interactive labels. The Office Action states that Nadaeu et al. further teaches wherein the composition comprises four non-labeled conventional deoxynucleotides. The Office Action acknowledges that Nadaeu et al. differs from the instant invention in that the reference does not teach wherein the composition further comprises a labeled conventional deoxynucleotide, and three other unlabeled chain terminators, wherein said labeled conventional deoxynucleotide, is incorporated into the oligonucleotide primer at a position corresponding to the predetermined nucleotide of the target in a sample. The Office Action states that Soderlund teaches a composition for detecting a nucleotide which comprises one or more conventional deoxynucleotides incorporated into the oligonucleotide primer, and optionally unlabeled chain terminators corresponding to the other three nucleotide residues, among other things. The Office Action concludes that it would have been obvious to one of ordinary skill in the art at the time of

the claimed invention to have been motivated to have modified the composition of Nadeau et al. with the composition of Soderlund et al. to further incorporate a labeled conventional deoxynucleotide and three other labeled chain terminators.

Applicants respectfully disagree.

Claim 18 is a claim dependent from claim 1, which is drawn to a composition for identifying a nucleotide at a predetermined position of a target polynucleotide in a sample, said composition comprising: (a) an oligonucleotide primer comprising a first sequence which hybridizes to said target polynucleotide immediately 3' of said nucleotide, and a second sequence which does not hybridize to said target polynucleotide in the presence of a third sequence; and (b) an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide primer, ***said oligonucleotide probe labeled with a first member of a pair of interactive labels.***

Applicants submit that Nadaeu et al. ***does not teach*** an element required in claim 18 of the present application, i.e., ***an oligonucleotide probe comprising said third sequence which hybridize to said second sequence of said oligonucleotide primer***. In contrast, Nadaeu et al. teaches an adapter sequence on the signal primer "is selected such that its ***complementary sequence*** will hybridize to the 3' end of the reporter probe..." (column 4, line 55), and that "[t]he sequence of the reporter probe 3' to the reporter moiety is selected to hybridize to the ***complement*** of the signal primer adapter sequence." (column 5, lines 3-6) Therefore, the probe in Nadeau et al. does not hybridize directly to the primer at all, it only hybridizes to the complemenary sequence of the primer. Even if one with ordinary skilled in the art would have been motivated to combine the teachings of Nadeau et al. and Soderlund et al., the combination of the two references will not result in the claimed invention, i.e., a composition for identifying a nucleotide at a predetermined position of a target polynucleotide in a sample, said composition comprising: (a) an oligonucleotide primer comprising a first sequence which hybridizes to said target polynucleotide immediately 3' of said nucleotide, and a second sequence which does not hybridize to said target polynucleotide in the presence of a third sequence; and (b) an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence

of said oligonucleotide primer, ***said oligonucleotide probe labeled with a first member of a pair of interactive labels.***

Therefore, claim 18 is not obvious over Nadeau et al. in view of Soderlund et al. Applicants respectfully request the 103(a) rejection on claim 18 be withdrawn.

Claim Rejections under 35 U.S.C. § 103(a) over Nadeau et al. in view of Goelet et al. and further in view of Sorge et al.

Claims 7 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nadaeu et al. in view of Goelet et al. as previously applied and further in view of Sorge et al. (WO 01/32887A1). The Office Action reiterates that Nadeau et al. in view of Goelet et al. teaches a composition for identifying a nucleotide at a predetermined position of a target polynucleotide, said composition comprising an oligonucleotide sequence which hybridizes to said target polynucleotide immediately 3' of the target sequence, a second sequence which does not hybridize to said target polynucleotide in presence of a third sequence; and *oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide sequence*, said oligonucleotide probe labeled with a first member of a pair of interactive labels, and wherein the composition further comprises one or more polynucleotide terminators incorporated in a template-dependent manner by a polynucleotide synthesis enzyme. The Office Action acknowledges that Nadaeu et al. in view of Goelet et al. differs from the instant invention in that the reference do not teach wherein the polynucleotide synthesis enzyme is a JDF-3 DNA polymerase, and that Sorge et al. discloses a JDF-3 DNA polymerase the use of the JDF-3 DNA polymerase in a template-dependent synthesis reaction. The Office Action concludes that one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the composition as taught by Nadeau et al. and Goelet et al. to incorporate a polynucleotide synthesis enzyme such as a JDF-3 DNA polymerase.

Applicants respectfully disagree.

Claims 7 and 25 are dependent from claims 1 and 20 respectively, and are drawn to a composition or kit for identifying a nucleotide at a predetermined position of a target

polynucleotide in a sample, said composition comprising: (a) an oligonucleotide primer comprising a first sequence which hybridizes to said target polynucleotide immediately 3' of said nucleotide, and a second sequence which does not hybridize to said target polynucleotide in the presence of a third sequence; and (b) an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide primer, ***said oligonucleotide probe labeled with a first member of a pair of interactive labels.***

Applicants submit that Nadaeu et al. ***does not teach*** an element required in claims 7 and 25 of the present application, i.e., ***an oligonucleotide probe comprising said third sequence which hybridize to said second sequence of said oligonucleotide primer***. In contrast, Nadaeu et al. teaches an adapter sequence on the signal primer "is selected such that its ***complementary sequence*** will hybridize to the 3' end of the reporter probe..." (column 4, line 55), and that "[t]he sequence of the reporter probe 3' to the reporter moiety is selected to hybridize to the ***complement*** of the signal primer adapter sequence." (column 5, lines 3-6) Therefore, the probe in Nadeau et al. does not hybridize directly to the primer at all, it hybridizes to the complementary sequence of the primer. Even if one with ordinary skilled in the art would have been motivated to combine the teachings of Nadeau et al. Goelet et al., and Sorge et al., the combination of the two references will not result in the claimed invention, i.e., a composition or a kit for identifying a nucleotide at a predetermined position of a target polynucleotide in a sample, said composition comprising: (a) an oligonucleotide primer comprising a first sequence which hybridizes to said target polynucleotide immediately 3' of said nucleotide, and a second sequence which does not hybridize to said target polynucleotide in the presence of a third sequence; and (b) an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide primer, ***said oligonucleotide probe labeled with a first member of a pair of interactive labels.***

Therefore, claims 7 and 25 are not obvious over Nadeau et al. in view of Goelet et al., further in view of Sorge et al. Applicants respectfully request the 103(a) rejection on claims 7 and 25 be withdrawn.

In view of the foregoing remarks, applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

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